Weight-Related Increases in Hypertension, Hypercholesterolemia, and Diabetes Risk in Normal Weight Male and Female Runners

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Background—Although 36% of US men and 42% of US women are of normal weight, the health implications of greater weight in ostensibly normal-weight individuals are seldom acknowledged.

Methods and Results—Self-reported physician-diagnosed incident diabetes, high cholesterol, and hypertension were compared with adult body mass index (BMI), and body circumferences in 29 139 male and 11 985 female nonsmoking runners followed prospectively for 7.7 and 7.4 years, respectively. Included among these were 20 731 men and 11 197 women who were of normal weight at baseline (BMI < 25 kg/m²). During follow-up, 2342 men (8.53%) and 499 women (4.26%) became hypertensive, 3330 men (12.2%) and 599 women (5.14%) were diagnosed with high cholesterol, and 197 men (0.68%) and 28 women (0.23%) became diabetic. Increasing BMI and waist circumference at baseline significantly increased the log odds for normal-weight men becoming hypertensive (P < 0.0001), hypercholesterolemic (P < 0.0001), and diabetic (P < 0.02), and for normal-weight women becoming hypertensive (P = 0.05). The log odds for being diagnosed with high cholesterol also increased with baseline BMI in normal-weight women (P < 0.05). Relative to men with BMI < 20 kg/m², the odds for being diagnosed with hypertension or high cholesterol increased by 45% (P = 0.05) and 64% (P = 0.002), respectively, for those with 20 ≤ BMI < 22.5 kg/m², and by 121% (P < 0.0001) and 135% (P < 0.0001), respectively, for those with 22.5 ≤ BMI < 25 kg/m². The odds for women with 22.5 ≤ BMI < 25 kg/m² developing hypertension or high cholesterol were 33% (P = 0.02) and 29% (P = 0.03) higher, respectively, than for women with 20 ≤ BMI < 22.5 kg/m², and 64% (P = 0.0007) and 41% (P = 0.008) higher, respectively, than women with BMI < 20 kg/m². Relative to men and women with BMI < 22.5 kg/m², the odds for developing diabetes during follow-up increased by 119% (P = 0.009) and 116% (P = 0.17), respectively, for those with 22.5 ≤ BMI < 25 kg/m².

Conclusions—Greater BMI and larger waist circumference increase the risks for hypertension, high cholesterol, and diabetes even among normal-weight nonsmoking runners, although overall risks remain relatively low vis-a-vis those for the overweight or obese. (Arterioscler Thromb Vasc Biol. 2007;27:1811-1819.)

Key Words: hypertension ▪ hypercholesterolemia ▪ diabetes ▪ exercise

Excess body weight increases the risk for left-ventricular hypertrophy, cardiovascular disease, type 2 diabetes mellitus, hypertension, stroke, lipoprotein disorders, osteoarthritis, cancers of the breast, uterus, prostate and colon, and total mortality. These risks have led to the classification of adult body mass index (BMI) between 18.5 and 24.9 kg/m² as normal weight, between 25.0 and 29.9 kg/m² as overweight, and ≥30 kg/m² as obese. Abdominal obesity in particular has been associated with coronary heart disease and conditions collectively described as metabolic syndrome. Waist circumference provides a convenient measure of abdominal obesity, with circumferences ≥ 89 cm in women and ≥ 102 cm in men classified as high risk for coronary heart disease and metabolic diseases.

Overweight and normal-weight men and women represent the majority of the population. The Third National Health and Nutrition Examination Survey (NHANES III) estimates that 36% of US men and 42% of US women are of normal weight.5 Overweight represents 42% of men and 28% of women, of whom 36% and 46%, respectively, have high blood cholesterol, and 34% and 39%, respectively, have high blood pressure.5 Type 2 diabetes mellitus may be relatively rare among normal-weight men and women, however high blood pressure (27% prevalence) and high blood cholesterol (23% prevalence) are not. Moreover, the dose-response relationship between BMI and high-blood cholesterol is primarily restricted to nonobese men and women.4

The health implications of excess body weight in ostensibly normal-weight individuals receive little attention in deference to those whose obesity is manifest, and impaired health is greatest. Most studies contrast disease risk for overweight and obese vis-a-vis normal weight without regard
to variations in risk within the normal range. However, attaining and preserving health should be personally important to the approximately 90 million US adults who are of normal weight. Moreover, emphasizing the health benefits of the optimal body weight in currently lean men and women could be more effective in preventing obesity than achieving sustained weight loss in those who are already overweight or obese.

This report examines prospectively the incidence of self-reported physician-diagnosed hypertension, high cholesterol, and diabetes in primarily normal-weight individuals. As participants of the National Runners’ Health Surveys,5,6 most exercised regularly at levels that exceeded guideline levels. The analyses suggest that despite their active lifestyle, greater body weights increased their risks for diabetes, hypertension, and high cholesterol. These data suggest the importance of avoiding weight gain even among ostensibly healthy-weight, physically active individuals.

Methods

The survey instruments and baseline characteristics of the National Runners’ Health Survey are described elsewhere.5,6 Briefly, a 2-page questionnaire, distributed nationally at races and to subscribers of a popular running magazine (Runners’ World, Emmaus, Pa), solicited information on demographics, running history, weight history, smoking habits, prior history of heart attacks and cancer, and medications for blood pressure, thyroid conditions, high cholesterol, and diabetes. The authors certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during this research. The study protocol was approved by the University of California Committee for the Protection of Human Subjects, and all participants signed committee-approved informed consents.

Participants reported whether a physician had told them they had high blood pressure, high cholesterol, or diabetes since their baseline questionnaire, and whether they took medications for these conditions subsequent to their baseline questionnaire. Self-reported hypertension and high cholesterol have been demonstrated by others as being generally reliable assessments introduced) show that running represents (with 95% confidence intervals) 4.26% of all vigorously intense activity in men and women, respectively, and 73.5 ± 23.7% and 69.4 ± 25.7% of their total reported leisure-time physical activity.

We employed logistic regression analyses to test whether BMI, body circumferences, or bra-cup size were related to the incidence of hypertension, diabetes, or high cholesterol. These included covariates for baseline age (age and age²), follow-up duration, exercise level (km/wk and km²/wk²), vegetarianism, and weekly intakes of alcohol, meat, fish, and fruit. If “P” represents the proportion of events (eg, diabetes), then the odds were computed as P/(1-P).

Logistic regression fits the coefficients for the linear equation \( \ln(P/(1-P)) = \alpha + \beta_1 x_1 + \beta_2 x_2 + \ldots \), where \( x_1, x_2, \ldots \) are the independent variables and \( \alpha, \beta_1, \ldots \) are the fitted coefficients. Rates per 1000 person years were computed by evaluating the logistic regression equations at the mean age and the reported mean weekly intakes of meat, fish, fruit, and alcohol. Results are presented for BMI as a continuous measure of weight standardized for height and as a categorical variable for the data partitioned by evenly spaced cut-points at 20, 22.5, 25, and 27.5 kg/m². These cut points were chosen to depict the dose-response relationship and not because they have particular clinical significance. The logistic regression analyses of baseline BMI as a continuous variable is described as linear trends in the log odds whereas the categorical results are expressed as odds ratios.

Results

The men were followed prospectively for (mean±SD) 7.74±1.84 years, and the women for 7.42±2.10 years. During follow-up, 2342 men (8.53%) and 499 women (4.26%) became hypertensive, 3330 men (12.2%) and 599 women (5.14%) were diagnosed with high cholesterol, and 197 men (0.68%) and 28 women (0.23%) became diabetic. Among those who were of normal weight (BMI <25 kg/m²) at baseline, 1314 men (6.64%) and 415 women (3.78%) became hypertensive, 2020 men (10.32%) and 518 women (4.75%) were diagnosed with high cholesterol, and 59 men (0.28%) and 15 women (0.13%) became diabetic.

Table 1 displays the sample characteristics by baseline BMI. In both sexes, higher baseline BMI was significantly associated with greater age, less exercise, broader waists, and slightly fewer years of education. Baseline BMI was also associated with diet. Servings of meat and fish per week increased with men’s and women’s BMIs, whereas in men, fruit intake declined and alcohol increased with BMIs. The decline in education with increasing weight is more statistically significant than clinically significant. The proportions of male and female vegetarians were inversely related to BMI. Vegetarians were 4-fold more prevalent in the leanest than the heaviest men and represented a full 20% of the leanest women. The length of follow-up was longer for women with BMIs <20 kg/m² than for those less lean, but otherwise, follow-up duration appeared unrelated to BMI. There was a strong inverse association of running distance and BMI, as has been reported and discussed previously for this cohort.5,6,12
BMI and Waist Circumference

Table 2 displays the logistic regression analyses for incident hypertension, high cholesterol, and diabetes with increasing adiposity. The intercepts were adjusted to the average exercise, meat, fish, fruit, and alcohol consumption, vegetarianism, and follow-up duration. In both men and women, higher baseline BMI and waist circumference predicted increased log odds for all 3 maladies. BMI remained a significant predictor of hypertension and high cholesterol when adjusted for waist circumference in both?
The probability ($P$) of an event during follow-up can be computed using the equation $P=\frac{1}{1+\exp\left(-\alpha-\beta(MI+\text{waist})\right)}$, where $\alpha$ is the intercept and $\beta$ and $\gamma$ are the coefficients for BMI and waist circumference, respectively. Significance levels for the logistic regression coefficients are coded: $^*P<0.05$, $^†P<0.01$, $^‡P<0.001$, and $^§P<0.0001$.

Despite all having ostensibly normal weight, men with higher baseline BMI or higher baseline waist circumference were significantly more likely to be diagnosed with high cholesterol during follow-up, and baseline BMI and waist circumference were independently predictive of high cholesterol. Normal-weight women with higher BMIs also had greater odds for being diagnosed with high cholesterol, but not those with greater waist circumferences.
Normal-weight men who were diagnosed with diabetes during follow-up had higher BMIs and larger waist circumferences at baseline than nondiabetics, although their separate independent contributions could not be distinguished as significant. Neither waist circumference nor BMI achieved statistical significance in predicting diabetes in women.

Additional analyses provided the odds ratios for specific BMI intervals at baseline (Figure 1). The significance levels correspond to whether the logistic regression coefficient differed significantly from that of the leanest men or women, or between BMI categories. The corresponding incidence rates adjusted to the mean age and the mean intakes of meat, fish, fruit, and alcohol per 1000 person years of follow-up are as follows: For BMI <20 kg/m², 20 ≤BMI <22.5 kg/m², 22.5 ≤BMI <25 kg/m², 25 ≤BMI <27.5 kg/m², and ≥27.5,BMI, the adjusted incident rates for hypertension were 4.3, 6.1, 9.1, 12.9, and 21.1, respectively, in men and 3.5, 4.2, 5.6, 10.1, and 12.4, respectively, in women; and the adjusted rates for incident high cholesterol were 7.5, 11.9, 16.4, 20.3, and 25.7, respectively, in men and 5.4, 5.8, 7.5, 9.9, and 14.7, respectively, in women. Incident diabetes in men per 1000 person years of follow-up were 0.2 for BMI <22.5 kg/m², 0.5 for 22.5 ≤BMI <25 kg/m², 1.3 for 25 ≤BMI <27.5 kg/m², and 4.1 for BMI ≥27.5 kg/m², after adjustment. The corresponding rates in women were 0.1, 0.3, 1.2, and 2.3 per 1000 person years of follow-up, respectively.

The figure shows that the odds ratios for hypertension increased monotonically from the leanest to heaviest men. Each incremental increase of 2.5 kg/m² was associated with a significant increase in the odds for hypertension. Having a desirable

![Figure 1](image-url)
BMI between 22.5 and 25 kg/m² meant having 55% greater odds of becoming hypertensive relative to men between 20 and 22.5 kg/m², and over twice the odds of those <20 kg/m².

There was also a progressive increase in women’s odds for becoming hypertensive. Even normal-weight women with BMIs between 22.5 and 25 kg/m² had significantly greater odds for becoming hypertensive; i.e., 33% greater than those with a BMI between 20 and 22.5 kg/m² and 64% greater than those lean women with a BMI <20 kg/m².

The dose–response curves of Figure 1 show that the odds for incident high cholesterol increased progressively with BMI in both men and women. In men, each 2.5 kg/m² increment in baseline BMI produced a significant increase in the odds for high cholesterol being diagnosed during follow-up. Normal-weight men with a BMI between 22.5 and 25 kg/m² had a 37% increase in their odds of acquiring high cholesterol relative to men with BMIs between 20 and 22.5 kg/m², and over twice the odds of those with BMIs under 20. Healthy-weight women with BMIs between 22.5 and 25 kg/m² had significantly greater odds for acquiring high cholesterol than leaner women.

As compared with the incremental increases in the odds for hypertension and high cholesterol, the odds for diabetes accelerated much more dramatically at higher BMI levels. Nevertheless, men with BMIs between 22.5 and 25 kg/m² were over twice as likely to become diabetic as were leaner men. At higher levels, the odds for diabetes tripled for each 2.5 kg/m² increment. Women’s odds for becoming diabetic increased dramatically in going from normal to moderately overweight.

The men’s relationships for waist circumferences are displayed in Figure 2, with and without adjustments for BMI. Contrasting the vertical scales of these graphs with those of the previous figure shows less impact of increasing waistline than increasing BMI on these metabolic diseases. Nevertheless, each 4-cm increment in men’s waist circumference produced significant incremental increases in the odds for both high cholesterol and hypertension (above 82 cm). Adjustment for exercise level had no affect on the odds ratios for hypertension and minor effects on the odds ratio for high cholesterol and diabetes. Most of the increases in odds were accounted for by BMI. Although diabetes risk was significantly higher in men with waistlines between 86 to 90 cm than with more narrowly waist men, the odds rose exponentially above 90 cm vis-à-vis <90 cm, but this again was largely attributable to higher BMI. Incident diabetes in women increased progressively with waist circumferences, and those with waistlines >70 cm had greater odds than those with waistlines <66 cm (Figure 3).

**Other Circumference Measures**

Finally, other baseline circumference measures also predicted incident hypertension, high cholesterol, and diabetes during follow-up, but not when adjusted for BMI. Specifically, hip circumference predicted incident hypertension (logistic coefficient per cm ± SE, men: 0.037 ± 0.005, women: 0.028 ± 0.007; P < 0.0001 for both), high cholesterol (men: 0.021 ± 0.004, P < 0.0001; women: 0.014 ± 0.007, P = 0.04), and diabetes (men: 0.050 ± 0.015, P = 0.001; women: 0.092 ± 0.022, P < 0.0001). Chest circumference also predicted hypertension (per cm, men: 0.041 ± 0.004, women: 0.039 ± 0.009; P < 0.0001 for both), high cholesterol (men: 0.022 ± 0.003, women: 0.032 ± 0.008; both P < 0.0001), and diabetes (men: 0.087 ± 0.010, women: 0.109 ± 0.026; both P = 0.0001). Women’s bra-cup size predicted hypertension (per size, 0.177 ± 0.058, P = 0.002), high cholesterol
Figure 3. Odds ratios for incident physician-diagnosed diabetes vs waist circumference in women followed prospectively for 7.4 years. Significance levels for difference in odds from the thinnest women are coded: *P < 0.05 and **P < 0.01, by logistic regression. Brackets designate 95% confidence intervals. The significance levels above the arrows are for the differences in odds between adjacent waist circumference categories unadjusted for BMI or exercise. All analyses were adjusted for age, follow-up duration, vegetarianism, and reported weekly intakes of meat, fish, fruit, and alcohol, and other variables as designated in the legend.

(0.186 ± 0.052, P = 0.0004), and diabetes (0.575 ± 0.226, P = 0.01). Except for an increased risk for high cholesterol with greater bra-cup size (adjusted logistic coefficient: 0.112 ± 0.056, P = 0.04), all became nonsignificant when adjusted for BMI.

Discussion

We have demonstrated that the odds for hypertension, high cholesterol, and diabetes all increase significantly with increasing BMI in both nonobese and normal-weight men and women. We also showed that larger waist circumference predicted greater odds for hypertension, high cholesterol, and diabetes in normal-weight men. This was true below the predicted greater odds for hypertension, high cholesterol, and diabetes all increase significantly with increasing BMI in both nonobese and normal-weight men and women. We have also shown that nonrunning men and women who maintained their weekly running distances within ±5 km/wk experienced smaller increases in both body weight and waist girth in proportion to the weekly distance run. We have also shown that the trajectory of weight gain with increasing age is greater at the 75th, 90th, and 95th percentiles of BMI than at lower percentiles of the BMI distribution. Others have also demonstrated the progressive increases in risks associated with increasing body weights among normal-weight individuals. For example, the concordance between body weight and blood pressure exists among lean Asian populations with low-overall blood pressure and where hypertension is largely nonexistent. The Nurses’ Health Study reported that compared with women having a BMI < 20 kg/m², the risk for hypertension among healthy-weight women increased 15% for 20 ≤ BMI < 21, 35% for 21 ≤ BMI < 22, 56% for 22 ≤ BMI < 23, 80% for 23 ≤ BMI < 24, 112% for 24 ≤ BMI < 25, 152% for 25 ≤ BMI < 26, 226% for 26 ≤ BMI < 28, and 310% for 28 ≤ BMI < 31. Compared with BMIs ≤ 22 kg/m², the risk for diabetes in healthy-weight women increased 2.1-fold for 22 ≤ BMI < 23, 3.6-fold for 23 ≤ BMI < 24, and 3.1-fold for 24 ≤ BMI < 25. Thereafter, diabetes risk in overweight women accelerated with higher BMIs, ie, a 5.2-fold increase for 25 ≤ BMI < 27, a 9.6-fold increase for 27 ≤ BMI < 29, and a 19-fold increase for 29 ≤ BMI < 31, compared with the leanest women.

Exercise, in addition to prudent dietary choices, may be key to achieving optimal body weight. Exercise prevents excess body weight in 2 ways. First, exercise attenuates age-related weight gain in both men and women. Population studies show that both body weight and abdominal fat increase with age. The increase in body weight and waist circumference from young adulthood to middle age is attenuated in proportion to the dose of vigorous exercise. We have shown that men and women runners followed for 7 years who maintained their weekly running distances within ±5 km/wk experienced smaller increases in both body weight and waist girth in proportion to the weekly distance run. We have also shown that the trajectory of weight gain with increasing age is greater at the 75th, 90th, and 95th percentiles of BMI than at lower percentiles of the BMI distribution. Vigorous physical activity appears to be most efficacious in the prevention of more extreme weight gain. This primary benefit of exercise requires emphasis because it is unlikely to be perceived directly but rather in relation to others who are not physically active and thus proceed inexorably to greater corpulence. The manifest importance of intervening to prevent weight gain is further supported by our unpublished data showing that the amount of weight gained by decreasing physical activity is greater than the amount of weight lost by comparable increases in activity, ie, becoming less physically active cannot be atoned for by resuming activity later.

Second, of primary significance to those who have become overweight is the acute loss of body weight from increased energy expenditure. Sedentary men randomly assigned to a program of vigorous exercise lose weight in proportion to the exercise dose, and the mean weight loss is significantly greater with them than with those who remain sedentary. We have also shown that nonrunning men and women who start running experience a net weight loss relative to those who remain sedentary over 7 years of follow-up.
is recommended as an adjunct to calorie restriction for producing weight loss, both because the combined strategy is more successful for long-term weight loss than is dieting alone, and to preserve lean muscle mass.27,28

Table 2 and Figures 2 and 3 show that when adjusted for BMIs, men’s waist circumferences were significantly associated with hypertension, high cholesterol, and diabetes, but that the associations were much diminished by the adjustments. Others also report that BMI accounts for most or all of the association with hypertension, hyperlipidemia, and diabetes, but not for other measures of visceral fat such as sagittal abdominal,29–31 which may be more precise. Our inability to demonstrate an independent association with waist circumference could relate to the greater imprecision of the self-reported waist circumference than BMI, which would attenuate its significance in the statistical analyses. In our data, greater hip and chest circumferences and bra-cup size also predicted increased odds for hypertension, high cholesterol, and diabetes, but not when adjusted for BMI (bra cup versus high cholesterol was the one exception). Thus, we could not confirm that the associations of hip or chest circumference or bust size with metabolic abnormalities were independent of BMI,32–34 nor that larger hip circumference has an opposite (protective) effect from total or abdominal adiposity.34–38 We caution that the statistical assumptions on which the adjustment depends may not strictly apply.12,5,6

The strength of our findings are derived from the prospective study design and consistency with prior reports and their unique focus on nonobese individuals (afflictions affecting the obese being well documented elsewhere) who largely meet or exceed public health recommendations for physical activity. Self-reported hypertension and high cholesterol have been demonstrated using repeated surveys and confirmed diagnosis on medical records8 to be generally reliable, and are trusted by the Nurses’ Health Study and other major cohorts.9,10,11 Our reliance on self-reported height, weight, and body circumference is supported by the reproducibility of these measures as demonstrated by our own repeated surveys and clinical measurements (Methods) and validation studies of others.39

Current public health guideline levels for desirable weight necessarily represent compromises between realistic expectations for sustained weights and the health consequences of excess body weights.26 The difficulty of producing sustained weight loss in obese individuals is well documented.2,27 Most men and women are lean in their youth and then gain weight as they age.40 Thus, for many, obesity begins with the accumulation of fat during a period of ostensibly healthy weight. Per kg of weight gain, the increase in incident cases of hypertension, high cholesterol, and diabetes is greater for the obese than for overweight individuals, and greater for overweight than normal-weight individuals. Nevertheless, a greater focus on the health benefits of optimal weight could serve the public health goals of obesity prevention by encouraging men and women to actively avoid weight gain while currently lean. Designating obesity as unhealthy does not require that we currently regard all normal weight as equally healthy. Public health priorities can recognize temporal trends toward greater obesity in Americans and still acknowledge the health benefits of promoting greater leanness among normal-weight men and women.

Sources of Funding
This work was supported in part by grants HL-45652, HL-072110, and DK066738 from the National Heart Lung and Blood Institute, and was conducted at the Ernest Orlando Lawrence Berkeley National Laboratory (Department of Energy DE-AC03-76SF00098 to the University of California).

Disclosures
None.

References


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Arterioscler Thromb Vasc Biol. 2007;27:1811-1819; originally published online May 17, 2007; doi: 10.1161/ATVBAHA.107.141853
Arteriosclerosis, Thrombosis, and Vascular Biology is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 1079-5642. Online ISSN: 1524-4636

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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